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Your Ref.: 09/859,503 Date: March 12, 2004

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From: Willem F. Gadiano

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ATTACHMENT/S:

1. **Amendment in connection with Reply Brief (13 Pages).**

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1. **Amendment in connection with Reply Brief (13 Pages).**

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Date: March 12, 2004

By: _____
Willem F. Gadiano, Registration No. 37,136

Docket No.: 4377.0062 **PATENT**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of	:	
Marc J. MCKENNON, et al.	:	Confirmation No.: 5034
Application No.: 09/859,503	:	Group Art Unit: 1624
Filed: May 18, 2001	:	Examiner: M. Berch

For: PYRIDOPYRIMIDINE COMPOUNDS AND THEIR USES

AMENDMENT

Commissioner for Patents
Washington, DC 20231

Sir:

This paper is concurrently submitted with a Reply Brief in the above-captioned patent application.

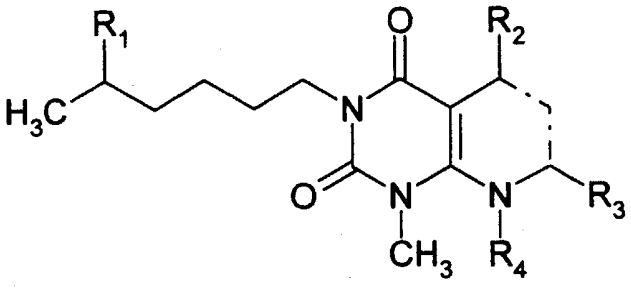
Amendments to the Claims are reflected in the listing of claims which begins on page 2 of this paper.

Remarks/Arguments begin on page 12 of this paper.

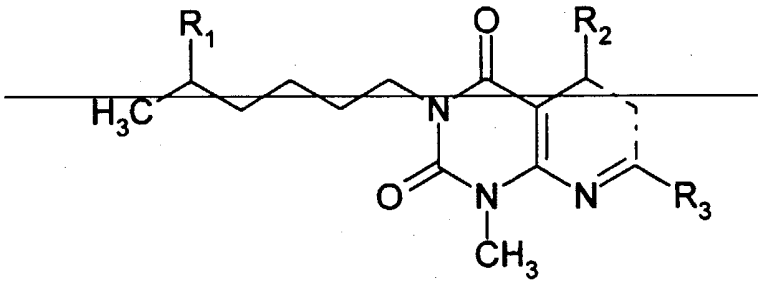
AMENDMENTS TO THE CLAIMS:

Upon entry, the following listing of claims will replace all prior versions and listings in the above-captioned patent application:

1. (Currently Amended) A therapeutic compound, including resolved enantiomers, diastereomers, tautomers, **and** salts ~~**and solvates**~~ thereof, having ~~**one of**~~ the following ~~**formulae**~~**formula**:



~~**or**~~



wherein:

R_1 is selected from a member of the group consisting of hydrogen, hydroxyl, methoxyl, acylamino group, cyano group, sulfo, sulfinyl, sulfhydryl (mercapto), sulfeno, sulfanilyl, sulfamyl, sulfamino, and phosphino, phosphinyl, phospho, phosphono and $-NR_aR_b$, wherein each of R_a and R_b may be the same or different and each is selected from the group consisting of

hydrogen and optionally substituted: $C_{(1-20)}$alkyl, $C_{(3-12)}$cycloalkyl, $C_{(2-20)}$alkenyl, $C_{(3-12)}$cycloalkenyl, $C_{(2-20)}$alkynyl, aryl, heteroaryl, and heterocyclic group;

R_2 and R_3 are independently selected from a member of the group consisting of halo, oxo, $C_{(1-20)}$alkyl, $C_{(1-20)}$hydroxyalkyl, ~~$C_{(1-20)}$thioalkyl,~~ $C_{(1-20)}$alkylthio, $C_{(1-20)}$alkylaminoalkyl, $C_{(1-20)}$aminoalkyl, $C_{(1-20)}$aminoalkoxyalkenyl, $C_{(1-20)}$aminoalkoxyalkynyl, $C_{(1-20)}$diaminoalkyl, $C_{(1-20)}$triaminoalkyl, $C_{(2-20)}$tetraaminoalkyl, $C_{(1-20)}$alkylamido, $C_{(1-20)}$alkylamidoalkyl, $C_{(1-20)}$amidoalkyl, $C_{(1-20)}$acetamidoalkyl, $C_{(2-20)}$alkenyl, $C_{(2-20)}$alkynyl, $C_{(1-20)}$alkoxyl, $C_{(1-20)}$alkoxyalkyl, $C_{(1-20)}$dialkoxyalkyl, and $-NR_aR_b$; and

R_4 may be hydrogen or an optionally substituted member of the group consisting of $C_{(1-20)}$alkyl, $C_{(3-12)}$cycloalkyl, $C_{(2-20)}$alkenyl, $C_{(3-12)}$cycloalkenyl, $C_{(2-20)}$alkynyl, aryl, heteroaryl, and heterocyclic group.

2. (Currently Amended) The therapeutic compound of claim 1, wherein R_2 and R_3 are independently selected from a member of the group consisting of hydrogen, halo, thio, oxo, $C_{(1-10)}$alkyl, $C_{(1-10)}$hydroxyalkyl, ~~$C_{(1-10)}$thioalkyl,~~ $C_{(1-10)}$alkylthio, $C_{(1-10)}$alkylamino, $C_{(1-10)}$alkylaminoalkyl, $C_{(1-10)}$aminoalkyl, $C_{(1-10)}$aminoalkoxyalkenyl, $C_{(1-10)}$aminoalkoxyalkynyl, $C_{(1-10)}$diaminoalkyl, $C_{(1-10)}$triaminoalkyl, $C_{(2-10)}$tetraaminoalkyl, $C_{(1-10)}$aminotrialkoxyamino, $C_{(1-10)}$alkylamido, $C_{(1-10)}$alkylamidoalkyl, $C_{(1-10)}$amidoalkyl, $C_{(1-10)}$acetamidoalkyl, $C_{(2-10)}$alkenyl, $C_{(2-10)}$alkynyl, $C_{(1-10)}$)alkoxyl, $C_{(1-10)}$alkoxyalkyl, and $C_{(1-10)}$dialkoxyalkyl.

3. (CANCELED)

4. (Currently Amended) The therapeutic compound of claim 37, wherein each of R_2 and R_3 is substituted with one or more members of the group consisting of hydroxyl, methyl,

carboxyl, furyl, furfuryl, biotinyl, phenyl, naphthyl, amino group, amido group, carbamoyl group, cyano group, sulfo, sulfonyl, sulfinyl, sulfhydryl, sulfeno, sulfanilyl, sulfamyl, sulfamino, phosphino, phosphinyl, phospho, phosphono, N-OH, $-Si(CH_3)_3$, $C_{(1-3)}$alkyl, $C_{(1-3)}$hydroxyalkyl, ~~$C_{(1-3)}$thioalkyl,~~ $C_{(1-3)}$alkylamino, benzyldihydrocinnamoyl group, benzoyldihydrocinnamido group, optionally substituted heterocyclic group and optionally substituted carbocyclic group.

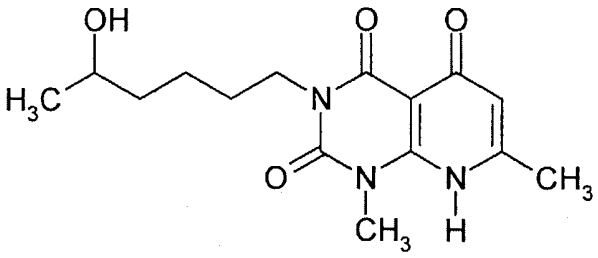
5. (Original) The therapeutic compound of claim 4, wherein the heterocyclic group or carbocyclic group is substituted with one or more members of the group consisting of halo, hydroxyl, nitro, SO_2NH_2, $C_{(1-6)}$alkyl, $C_{(1-6)}$haloalkyl, $C_{(1-6)}$alkoxyl, $C_{(1-11)}$alkoxyalkyl, $C_{(1-6)}$alkylamino, and $C_{(1-6)}$aminoalkyl.

6. (Original) The therapeutic compound of claim 4, wherein the heterocyclic group is a member selected from the group consisting of acridinyl, aziridinyl, azocinyl, azepinyl, benzimidazolyl, benzodioxolanyl, benzofuranyl, benzothiophenyl, carbazole, 4a H-carbazole, chromanyl, chromenyl, cinnolinyl, decahydroquinolinyl, dioxoindolyl, furazanyl, furyl, furfuryl, imidazolidinyl, imidazolinyl, imidazolyl, 1H-indazolyl, indolenyl, indolinyl, indolizinyl, indolyl, 3H-indolyl, isobenzofuranyl, isochromanyl, isoindolinyl, isoindolyl, isoquinolinyl, isothiazolyl, isoxazolyl, morpholinyl, naphthyridinyl, octahydro-isoquinolinyl, oxazolidinyl, oxazolyl, oxiranyl, perimidinyl, phenanthridinyl, phenanthrolinyl, phenarsazinyl, phenazinyl, phenothiazinyl, phenoxathiinyl, phenoxazinyl, phthalazinyl, piperazinyl, piperidinyl, 4-pipendonyl, piperidyl, pteridinyl, purinyl, pyranyl, pyrazinyl, pyrazolidinyl, pyrazolinyl, pyrazolyl, pyridazinyl, pyndinyl, pyridyl, pyndyl, pyrimidinyl, pyrrolidinyl, 2-pyrrolidonyl, pyrrolonyl, pyrrolyl, 2H-pyrrolyl, quinazolinyl, 4H-quinolizinyl, quinolinyl, quinoxalinyl, quinuclidinyl, β-carbolinyl, tetrahydrofuranyl, tetrahydroisoquinolinyl, tetrahydroquinolinyl,

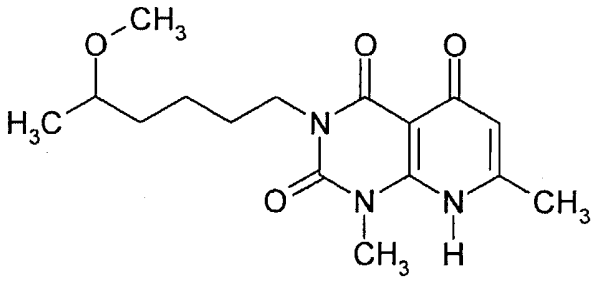
tetrazolyl, 6H-1,2,5-thiadiazinyl, 2H-,6H-1,5,2-dithiazinyl, thianthrenyl, thiazolyl, thienyl, thiophenyl, triazinyl, xanthenyl and xanthinyl.

7. (Previously presented) The therapeutic compound of claim 4, wherein the carbocyclic group is a member selected from the group consisting of adamantyl, anthracenyl, benzyl, bicyclo[2.2.1] heptanyl, bicyclo[2.2.1]hexanyl, bicyclo[2.2.2]octanyl, bicyclo[3.2.0]heptanyl, bicyclo[4.3.0]-nonanyl, bicyclo[4.4.0]decanyl, biphenyl, biscyclooctyl, cyclobutyl, cyclobutenyl, cycloheptyl, cycloheptenyl, cyclohexanedionyl, cyclohexenyl, cyclohexyl, cyclooctanyl, cyclopentadienyl, cyclopentanedionyl, cyclopentenyl, cyclopentyl, cyclopropyl, decalinyl, 1,2-diphenylethanyl, indanyl, 1-indanonyl, indenyl, naphthyl, napthlalenyl, phenyl, resorcinolyl, stilbenyl, tetrahydronaphthyl, tetralinyl, tetralonyl, and tricyclododecanyl.

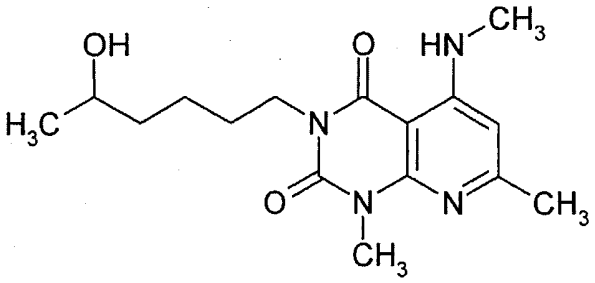
8. (Currently Amended) A compound, including resolved enantiomers, diastereomers, tautomers, **and** salts ~~**and solvates**~~ thereof, having the formula:



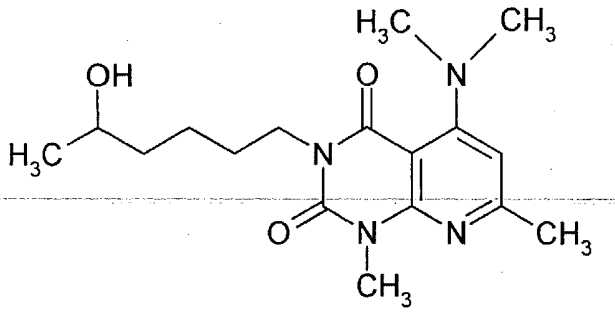
9. (Currently Amended) A compound, including resolved enantiomers, diastereomers, tautomers, **and** salts ~~**and solvates**~~ thereof, having the formula:



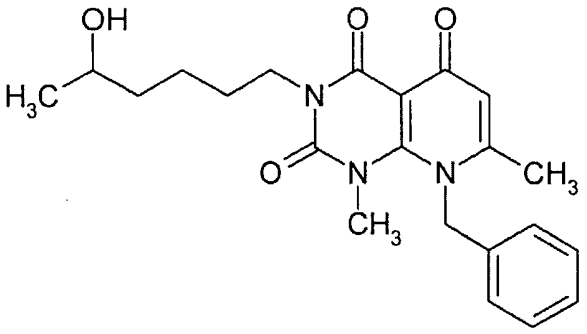
10. (Currently Amended) A compound, including resolved enantiomers, diastereomers, tautomers, **and** salts ~~**and solvates**~~ thereof, having the formula:



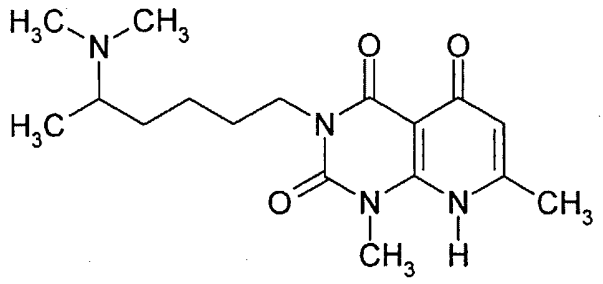
11. (Currently Amended) A compound, including resolved enantiomers, diastereomers, tautomers, **and** salts ~~**and solvates**~~ thereof, having the formula:



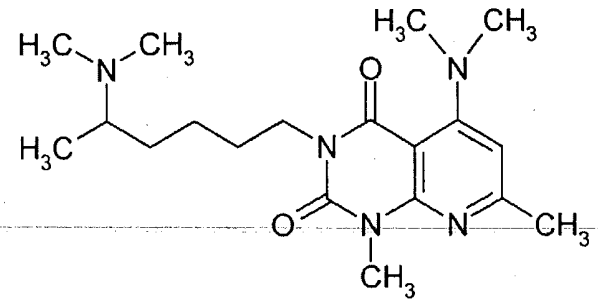
12. (Currently Amended) A compound, including resolved enantiomers, diastereomers, tautomers, **and** salts ~~**and solvates**~~ thereof, having the formula:



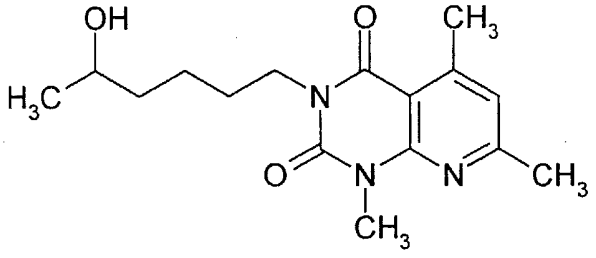
13. (Currently Amended) A compound, including resolved enantiomers, diastereomers, tautomers, **and** salts ~~**and solvates**~~ thereof, having the formula:



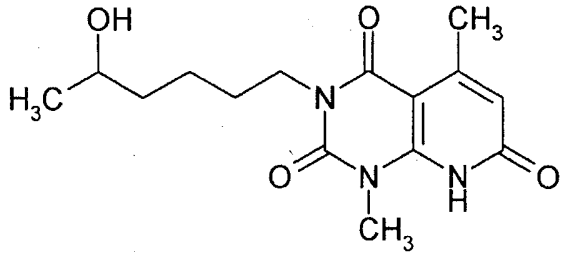
14. (Currently Amended) A compound, including resolved enantiomers, diastereomers, tautomers, **and** salts ~~**and solvates**~~ thereof, having the formula:



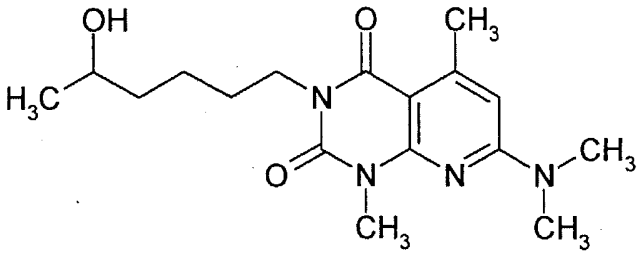
15. (Currently Amended) A compound, including resolved enantiomers, diastereomers, tautomers, **and** salts ~~**and solvates**~~ thereof, having the formula:



16. (Currently Amended) A compound, including resolved enantiomers, diastereomers, tautomers, **and** salts ~~**and solvates**~~ thereof, having the formula:



17. (Currently Amended) A compound, including resolved enantiomers, diastereomers, tautomers, **and** salts ~~**and solvates**~~ thereof, having the formula:



18. (Original) A pharmaceutical composition comprising the compound of claim 1 in admixture with a pharmaceutically acceptable carrier, adjuvant or vehicle.

Claims 19 to 27. (CANCELED)

28. (Currently Amended) A method for treating a T1 cell-mediated inflammatory response in a mammal in need of such treatment, the method comprising administering to the mammal a therapeutically effective amount of the compound of claim 1~~, wherein said compound is capable of inhibiting an IL-12 mediated cellular process or activity, thereby inhibiting the inflammatory response~~.

29. (Original) The method of claim 28, wherein the inflammatory response is associated with a disease or condition selected from the group consisting of chronic inflammatory disease, chronic intestinal inflammation, arthritis, psoriasis, asthma and autoimmune disorders.

30. (Original) The method of claim 28, wherein said autoimmune disorder is selected from Type-1 IDDM, multiple sclerosis, rheumatoid arthritis, uveitis, inflammatory bowel disease, lupus disorders, and acute and chronic graft-versus-host disease.

31. (Original) The method of claim 28, wherein said mammal is a human.

32. (Currently Amended) A method for treating a T2 cell-mediated anti-inflammatory response in a mammal in need of such treatment, the method comprising administering to the mammal a therapeutically effective amount of the compound of claim 1~~, wherein said compound is capable of inhibiting an IL-4 mediated cellular process or activity, thereby inhibiting anti-inflammatory response~~.

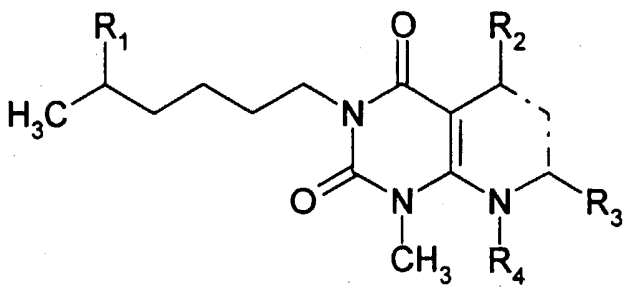
33. (Original) The method of claim 32, wherein the anti-inflammatory response is associated with a disease or condition selected from the group consisting of asthma, atopic dermatitis, hay fever, eczema, urticaria and food allergy.

34. (Original) The method of claim 33, wherein said disease is asthma.

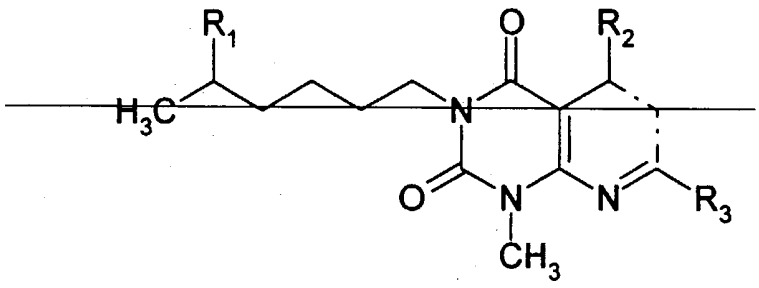
35. (Original) The method of claim 32, wherein said mammal is a human.

36. (Currently Amended) A method for treating NIDDM comprising a step of administering to a subject in need of such treatment a therapeutically effective amount of ~~a~~ **the** compound of claim 1.

37. (Currently Amended) A therapeutic compound, including resolved enantiomers, diastereomers, tautomers, **and** salts ~~and solvates~~ thereof, having ~~one of~~ the ~~following formulae~~ **formula**:



or



wherein:

R_1 is selected from a member of the group consisting of hydrogen, hydroxyl, methoxyl, acylamino group, cyano group, sulfo, sulfonyl, sulfinyl, sulfhydryl (mercapto), sulfeno, sulfanilyl, sulfamyl, sulfamino, phosphino, phosphinyl, phospho, phosphono and $-NR_aR_b$, wherein each of R_a and R_b may be the same or different and each is selected from the group consisting of hydrogen and optionally substituted: $C_{(1-20)}$alkyl, $C_{(3-12)}$cycloalkyl, $C_{(2-20)}$alkenyl, $C_{(3-12)}$cycloalkenyl, $C_{(2-20)}$alkynyl, aryl, heteroaryl, and heterocyclic group;

R_2 and R_3 are independently selected from a unsubstituted or substituted member of the group consisting of methyl, ethyl, oxo, isopropyl, n-propyl, isobutyl, n-butyl, t-butyl, 2-hydroxyethyl, 3-hydroxypropyl, 3-hydroxy-n-butyl, 2-methoxyethyl, 4-methoxy-n-butyl, 5-hydroxyhexyl, 2-bromopropyl, 3-dimethylaminobutyl, 4-chloropentyl, methylamino, amino-methyl, and methylphenyl; and

R_4 may be hydrogen or an optionally substituted member of the group consisting of $C_{(1-20)}$alkyl, $C_{(3-12)}$cycloalkyl, $C_{(2-20)}$alkenyl, $C_{(3-12)}$cycloalkenyl, $C_{(2-20)}$alkynyl, aryl, heteroaryl, and heterocyclic group.

REMARKS/ARGUMENTS

Solely in an effort to simplify further the issues on appeal and advance prosecution, Applicants have canceled claims 19-27 without prejudice or disclaimer of the subject matter they contain, and have amended claims 1, 2, 4, 8-17, 28, 32, 36 and 37 to encompass infringing subject matter.

Entry and favorable consideration of the above claim amendment(s) is believed to be appropriate and is hereby respectfully requested because such claim amendments: (a) place the application in condition for allowance; (b) do not raise any new issues requiring further search and/or consideration (since the amendments amplify or address issues previously discussed throughout the prosecution); and/or (c) do not present any additional claims without canceling a corresponding number of finally rejected claims. Upon entry of the above claim amendments, claims 1, 2, 4-18 and 28-38 will be pending. It is believed that the above claim amendments place this application in condition for allowance. Applicants reserve the right to file continuing applications for any canceled or unclaimed subject matter disclosed in the above-captioned patent application.

Please grant any extensions of time deemed necessary. The Commissioner is hereby authorized to charge any deficiency in the small-entity fee(s) filed, or asserted to be filed, or which should have been filed herewith (or with any paper filed hereafter) to Deposit Account No. **14-1140**.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: _____

Willem F. Gadiano
Reg. No. 37,136

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Date: March 12, 2004

By: _____
Willem F. Gadiano, Registration No. 37,136